PERSPECTIVES

Plasticity of neuronal excitability *in vivo*

Dominique Debanne[1,2]
[1]*INSERM U641, Marseille, 13344 France*
[2]*Université de la Méditerranée, Faculté de Médecine secteur nord, IFR 11, Marseille, 13344 France*

Email: dominique.debanne@univmed.fr

For years, long-lasting plasticity of synaptic transmission was the favourite mechanism to account for information storage in the brain. While bidirectional long-term synaptic plasticity is computationally appealing (in part because of synapse-specific changes among a large array of inputs), it is not the whole story. Recent evidence indicates that the neuronal message is also persistently filtered through regulation of voltage-gated ion channels. Excitatory postsynaptic potentials (EPSPs) measured at the axon hillock result from a tight interplay between synaptic and intrinsic voltage-gated conductances that either amplify or attenuate the synaptic potentials (review in Spruston, 2008). Any modifications in this fragile equilibrium may in turn facilitate or diminish the probability that a given synaptic input triggers an action potential. For instance, induction of long-term synaptic potentiation (LTP) in CA1 hippocampal neurons down-regulates A-type K^+ (Frick *et al.* 2004) and hyperpolarization-activated cationic (H) currents (Campanac *et al.* 2008) in the dendrites, and in turn facilitates the generation of an action potential by the EPSP. In paired recordings of connected neurons, LTP is associated with an increase in excitability of the presynaptic neuron that results from a facilitation of the transient sodium current (Ganguly *et al.* 2000). Independently of synaptic activation, rapid elevation in neuronal excitability may also be induced by directly conditioning the neuron with repeated action potential bursting of the recorded neuron (Cudmore & Turrigiano, 2004). Here, the global increase in excitability is accompanied by modifications in the threshold for action potential generation. Plasticity of neuronal excitability may therefore be defined as the persistent modification of intrinsic electrical properties of a neuron induced by neuronal (action potential firing) or synaptic activity. It is mediated by changes in the expression level or biophysical properties of ion channels and may thus alter a large range of functional processes such as dendritic integration, spike generation, signal propagation in the dendrite and the axon, and regulation of plasticity thresholds.

Most of the recent advances in understanding induction and expression mechanisms of intrinsic plasticity come from *in vitro* studies on brain slices or cultures of dissociated neurons. Less attention has been devoted to the search for cellular excitability correlates of learning and memory in the mammalian brain. Eye-blink conditioning in the cat or the rabbit provides, however, representative examples of learning-driven changes in neuronal excitability in hippocampal, cerebellar and cortical neurons. In conditioned animals, neurons that are active during conditioning display *in vitro* excitability that is significantly higher than that of neurons recorded from naive or pseudo-conditioned animals (Disterhoft *et al.* 1986). Changes in excitability of physiologically characterized neurons *in vivo* remain, however, uncertain because excitability changes were generally measured in separate populations of neurons before and after conditioning (Aou *et al.* 1992).

In this issue of *The Journal of Physiology*, Paz and co-workers filled the gap by providing direct evidence that rat motor cortex neurons recorded intracellularly *in vivo* express a long-lasting increase in excitability following cellular conditioning (Paz *et al.* 2009). The authors accomplished here a technical tour-de-force by obtaining stable intracellular recordings from identified L5 neurons in anaesthetized rats. Excitability changes were quantified by current–firing curves established before and after conditioning which consisted of repeated postsynaptic bursting at 30 Hz. Two main parameters are classically measured in input–output curves: the firing threshold and the gain (Carvalho & Buonomano, 2009). Changes in firing threshold signify modification in excitability drive (e.g. sodium current) whereas modifications in the gain usually indicate regulation of the excitability brake (e.g. after-hyperpolarizing potential). Consistent with previous *in vitro* findings (Cudmore & Turrigiano, 2004), repeated postsynaptic bursting induced by direct injection of depolarizing current in the neuron produced a long-lasting (> 30 min) increase in excitability in the great majority of changes (Paz *et al.* 2009; Fig. 1). The induction mechanisms have not been characterized here because of the complexity of the experiment, but one may suppose that action potential bursting triggers postsynaptic calcium influx that will activate an enzymatic cascade controlling the activity of one (or several) ion channel(s). In fact, the excitability changes displayed heterogeneous behaviour. In one-third of cases, an increase in excitability was associated with a reduction in the firing threshold. In the second third, the gain of the input–output curve was altered and in the remaining third, both changes were observed, suggesting multiple expression mechanisms.

The report by Paz and colleagues extends our knowledge of the potential of functional plasticity observed in the whole brain *in vivo*. Furthermore, this study will certainly motivate many other investigations in the future because several major questions are pending. Here, intrinsic

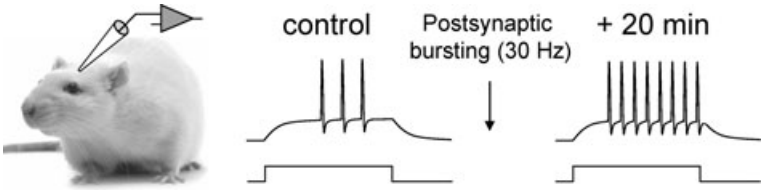

Figure 1
Repeated bursting of layer 5 pyramidal neuron induces long-term potentiation of intrinsic excitability in rat cortical motor neurons *in vivo*.

© 2009 The Author. Journal compilation © 2009 The Physiological Society
DOI: 10.1113/jphysiol.2009.175448

plasticity was induced by postsynaptic bursting in the recorded neuron but the effects of physiologically relevant synaptic stimulation remain unknown. In addition, the precise conditions allowing induction of a persistent decrease in excitability will require clarification. Finally, the potential of intrinsic plasticity in other neuronal types including pyramidal and non-pyramidal cells must be defined.

References

Aou S, Woody CD & Birt D (1992). *J Neurosci* **12**, 560–569.

Campanac E, Daoudal G, Ankri N & Debanne D (2008). *J Neurosci* **28**, 8635–8643.

Carvalho TP & Buonomano DV (2009). *Neuron* **61**, 774–785.

Cudmore RH & Turrigiano GG (2004). *J Neurophysiol* **92**, 341–348.

Disterhoft JF, Coulter DA & Alkon DL (1986). *Proc Natl Acad Sci U S A* **83**, 2733–2737.

Frick A, Magee J & Johnston D (2004). *Nat Neurosci* **7**, 126–135.

Ganguly K, Kiss L & Poo MM (2000). *Nat Neurosci* **3**, 1018–1026.

Paz JT, Mahon S, Tiret P, Genet S, Delord B & Charpier S (2009). *J Physiol* **587**, 3189–3205.

Spruston N (2008). *Nat Rev Neurosci* **9**, 206–221.

© 2009 The Author. Journal compilation © 2009 The Physiological Society